

- Lis® single-use fixed-bed bioreactor, from bench-scale to industrial scale. 7 (Suppl 6), 59-60. 2013. BMC Proceedings. Ref Type: Generic
- [0118] Meuwly, F., P. A. Ruffieux, A. Kadouri, and S. U. von, 2007 Packed-bed bioreactors for mammalian cell culture: bioprocess and biomedical applications. *Biotechnol. Adv.* 25: 45-56.
- [0119] Salmon, F., K. Grosios, and H. Petry, 2014 Safety profile of recombinant adeno-associated viral vectors: focus on alipogene tiparvovec (Glybera®). *Expert. Rev. Clin. Pharmacol.* 7: 53-65.
- [0120] Segura, M. M., A. Garnier, Y. Durocher, H. Coelho, and A. Kamen, 2007 Production of lentiviral vectors by large-scale transient transfection of suspension cultures and affinity chromatography purification. *Biotechnol. Bioeng.* 98: 789-799.
- [0121] Stacey, G. N., and O. W. Merten, 2011 Host cells and cell banking. *Methods Mol. Biol.* 737: 45-88.
- [0122] Vellinga, J., J. P. Smith, A. Lipiec, D. Majhen, A. Lemckert et al. 2014 Challenges in manufacturing adeno-viral vectors for global vaccine product deployment. *Hum. Gene Ther.* 25: 318-327.
- [0123] Wu, S. C., G. Y. Huang, and J. H. Liu, 2002 Production of retrovirus and adenovirus vectors for gene therapy: a comparative study using microcarrier and stationary cell culture. *Biotechnol. Prog.* 18: 617-622.
1. A method for the production of a recombinant biological product, comprising:
    - (b) obtaining suspension-adapted cells; and
    - (c) inoculating the suspension-adapted cells obtained in (b) into a bioreactor having a carrier providing a surface area for adherent cell culture.
  2. The method according to claim 1, further comprising:
    - (a) before said obtaining step and before said inoculating step, expanding the suspension-adapted cells in non-adherent mode.
  3. The method of claim 1, further comprising:
    - (d) exposing said cells to a factor promoting adherence, in an amount effective to promote adherence, whereby after said inoculating step said cells adhere to said carrier in said bioreactor.
  4. The method of claim 3, further comprising:
    - (e) after said cells adhere to the carrier, introducing into said cells a transgene.
  5. The method of claim 4, where said transgene is introduced into said cells by a viral vector.
  6. A method according to claim 1, wherein said cells express a transgene in said bioreactor.
  7. The method of claim 6, wherein said transgene is introduced into said cells after said inoculating step.
  8. A method according to claim 6, wherein the transgene codes for a therapeutic protein.
  9. The method according to claim 8, where the therapeutic protein comprises a polypeptide selected from the group consisting of: short-form VEGF-D3, endostatin, angiostatin, thymidine kinase, human interferon alpha-2b, ABCA4, ABCD-1, myosin VIIA, cyclooxygenase-2, PGF2-alpha receptor, dopamine, human hemoglobin subunit beta and an antibody subunit.
  10. The method of claim 6, wherein the transgene codes for a polypeptide comprising a viral component selected from the group consisting of: viral vector, viral-like particle, virus and viral vaccine.
  11. The method of claim 10, where the polypeptide comprises a component of a viral vector.
  12. The method of claim 11, where the viral vector is lentiviral.
  13. The method of claim 11, wherein the polypeptide comprises at least about  $1 \times 10^{17}$  viral vector particles.
  - 14-15. (canceled)
  16. A method comprising:
    - (a) obtaining cells;
    - (b) introducing the cells into a culture vessel having a surface area for adherent cell culture;
    - (c) exposing the cells to a factor to promote adherent culture, whereby after said inoculating step the cells adhere to at least part of the surface area; and
    - (d) after the cells adhere to the surface area, transfecting the cells at a pH of less than 7.2 with a transgene.
  17. A method comprising:
    - (a) obtaining cells;
    - (b) inoculating the cells into a bioreactor having a carrier providing a surface area for adherent cell culture;
    - (c) exposing the cells to a factor to promote adherent culture, whereby after said inoculating step the cells adhere to at least part of the surface area of the carrier in the bioreactor; and
    - (d) after the cells adhere to the carrier in the bioreactor, transfecting the cells with a viral vector carrying a transgene.
  18. The method according to claim 3, wherein said factor comprises a compound selected from the group consisting of: foetal bovine serum, fibronectin, collagen, laminin, calcium ions, proteoglycans of the extracellular matrix, non-proteoglycan polysaccharides of the extracellular matrix, and combinations thereof.
  19. A method according to claim 5, wherein the Multiplicity of Infection (MOI) for said transfection is not more than about 10 viral particles per cell.
  20. Use of suspension-adapted cells in a method for the production of a recombinant biological product; wherein said suspension-adapted cells have been expanded in a suspension cell culture; and wherein said method comprises inoculating the expanded cells obtained from the suspension culture into an bioreactor, and culturing the expanded cells in adherent mode to produce the recombinant biological product.
  21. A method comprising:
    - a. Obtaining an adherent-culture bioreactor having i) a carrier providing a surface area for adherent cell culture and ii) cell culture medium, and then
    - b. On said carrier, culturing cells adherent to said carrier, whereby said cells express an expression product, and then
    - c. Removing said cell culture medium from said micro-carrier, and then
    - d. Rinsing said carrier to obtain said expression product.
  22. The method of claim 21, further comprising:
    - a. Obtaining said expression product from said culture medium.
  23. The method of claim 16, where the culture vessel is an adherent culture bioreactor.
  24. method of purifying viral vector made by producer cells, comprising: manufacturing viral vector in producer cells in a liquid medium, and then adding lysis detergent and salt to the liquid medium in an amount sufficient to reduce the formation of precipitation in the medium.